

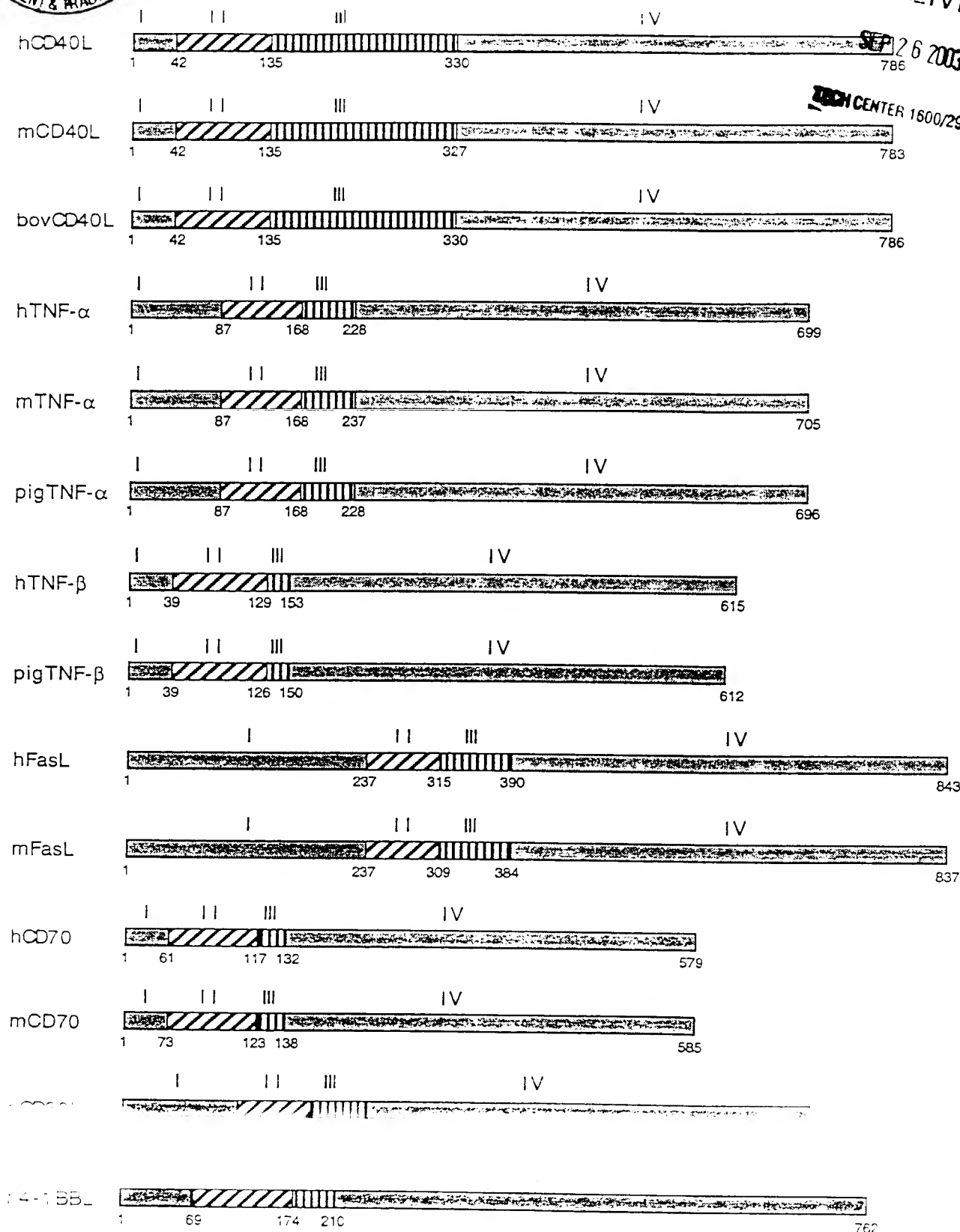


NOVEL EXPRESSION VECTORS CONTAINING ACCESSORY MOLECULE
LIGAND GENES AND THEIR USE FOR IMMUNOMODULATION AND
TREATMENT OF MALIGNANCIES AND AUTOIMMUNE DISEASES
Inventors: Thomas Kippel et al. Serial No.: 08/981,272
Filing Date: December 1, 1997 Att. Docket No.: 041673-2065

RECEIVED

SEP 26 2003

TECH CENTER 1600/2900



DOMAINS I - Cytoplasmic Domain II - Transmembrane Domain III - Extracellular Domain IV - C-terminal
Protein I - hCD40L II - mCD40L III - bovCD40L IV - hTNF- α V - mTNF- α VI - pigTNF- α VII - hTNF- β VIII - pigTNF- β IX - hFasL X - mFasL XI - hCD70 XII - mCD70 XIII - hCD27 XIV - hCD27

Figure 1



RECEIVED
 SEP 26 2003
 TECH CENTER 1800/2900

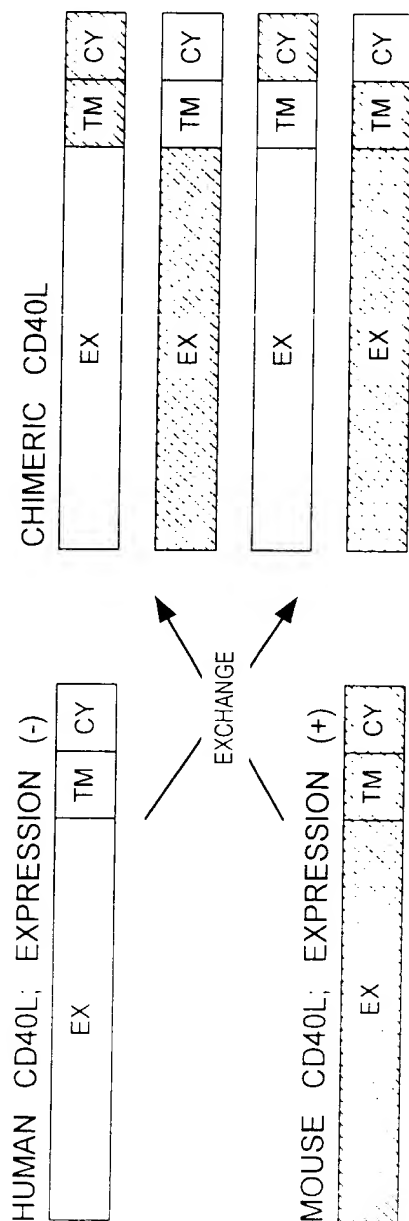
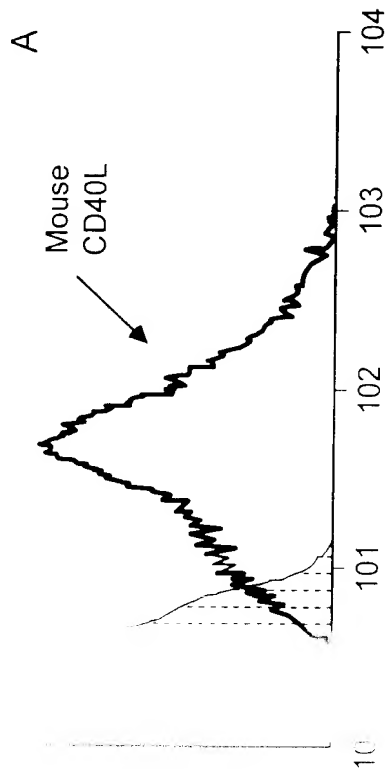


Figure 2



HeLa



CLL

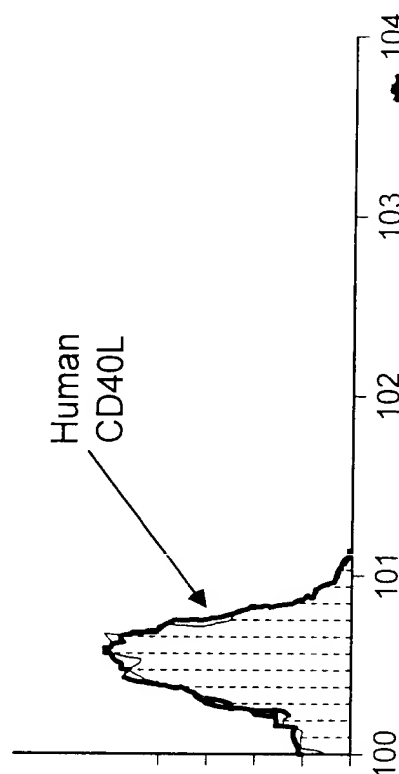
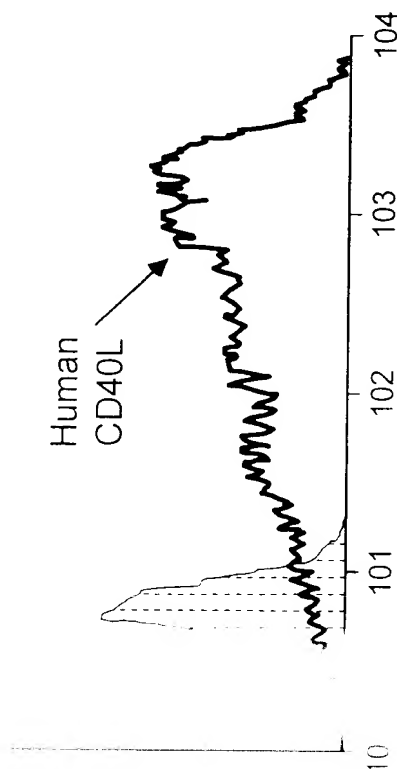
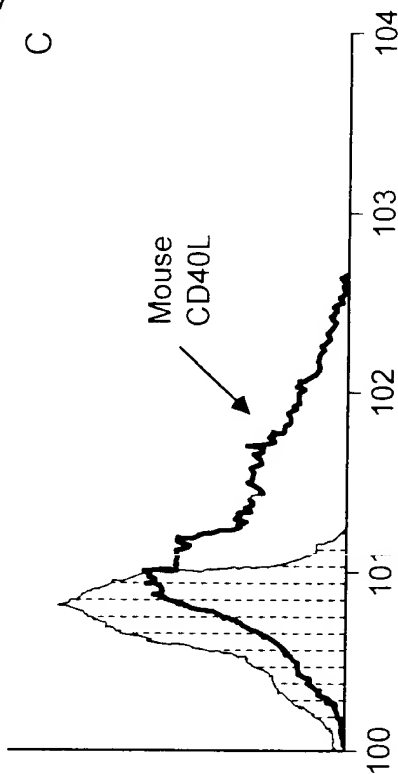
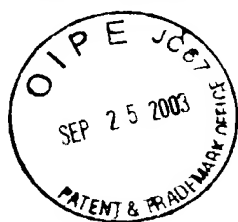


Figure 3

RECEIVED

SEP 26 2003

TECH. CENTER 1600/2900



NOVEL EXPRESSION VECTORS CONTAINING ACCESSORY MOLECULE
LIGAND GENES AND THEIR USE FOR IMMUNOMODULATION AND
TREATMENT OF MALIGNANCIES AND AUTOIMMUNE DISEASES
Inventors: Thomas Kipps, et al. Serial No. 08/982,172
Filing Date: December 1, 1997, Atty. Docket No. 041673-2069

RECEIVED

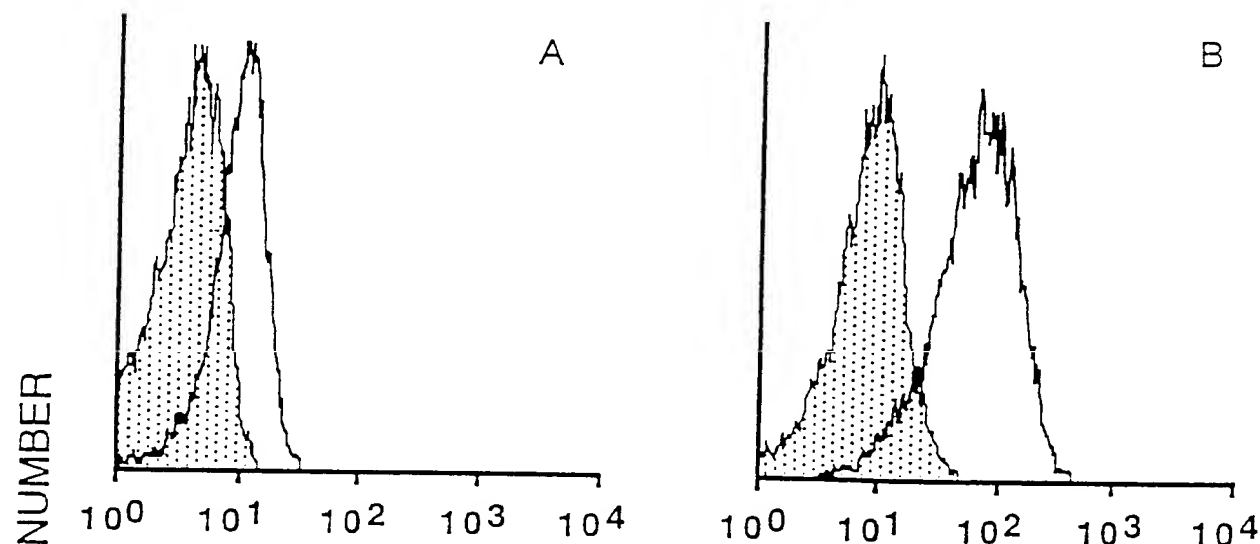
SEP 26 2003

TECH CENTER 1600/C300

NONINFECTED

+mCD40-L ADENOVIRUS

CD54 EXPRESSION



CD80 EXPRESSION

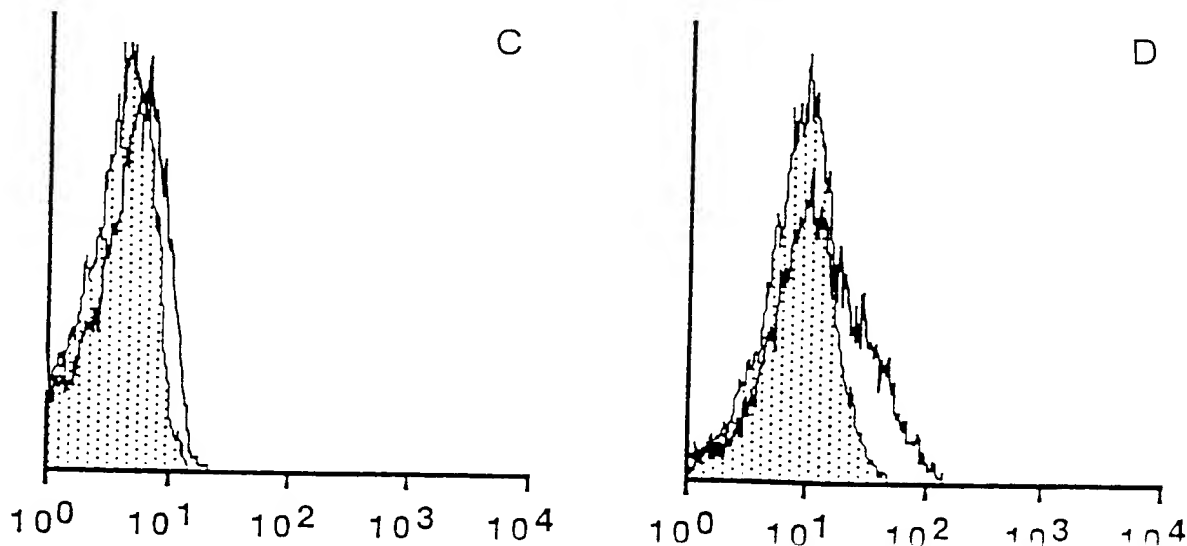


Figure 4



RECEIVED
SEP 26 2003
TECH CENTER 1600/2900

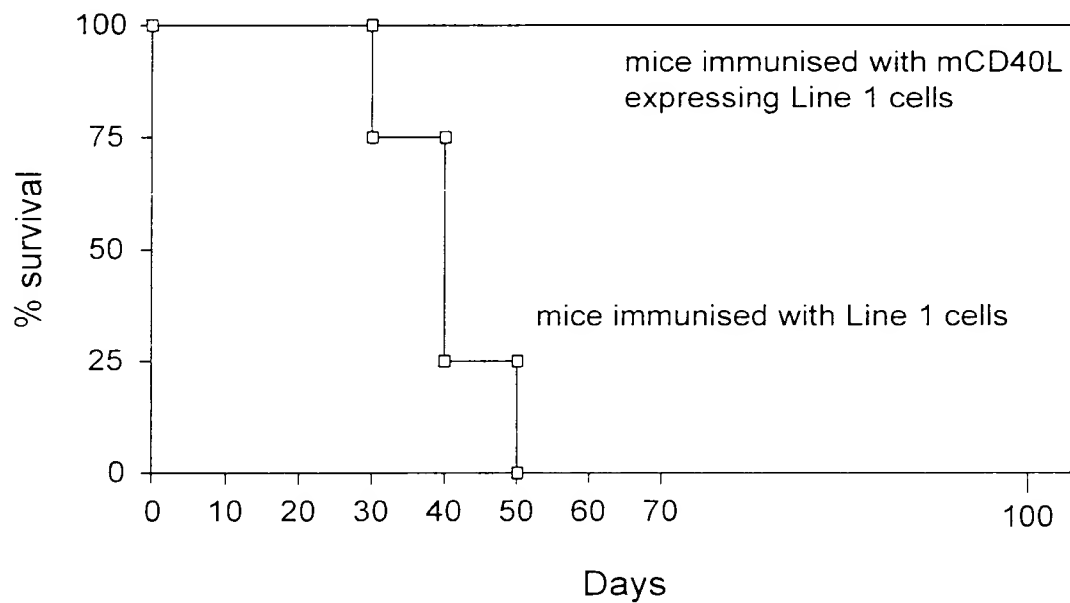


Figure 7



RECEIVED
 SEP 26 2003

TECH CENTER 1600/2900

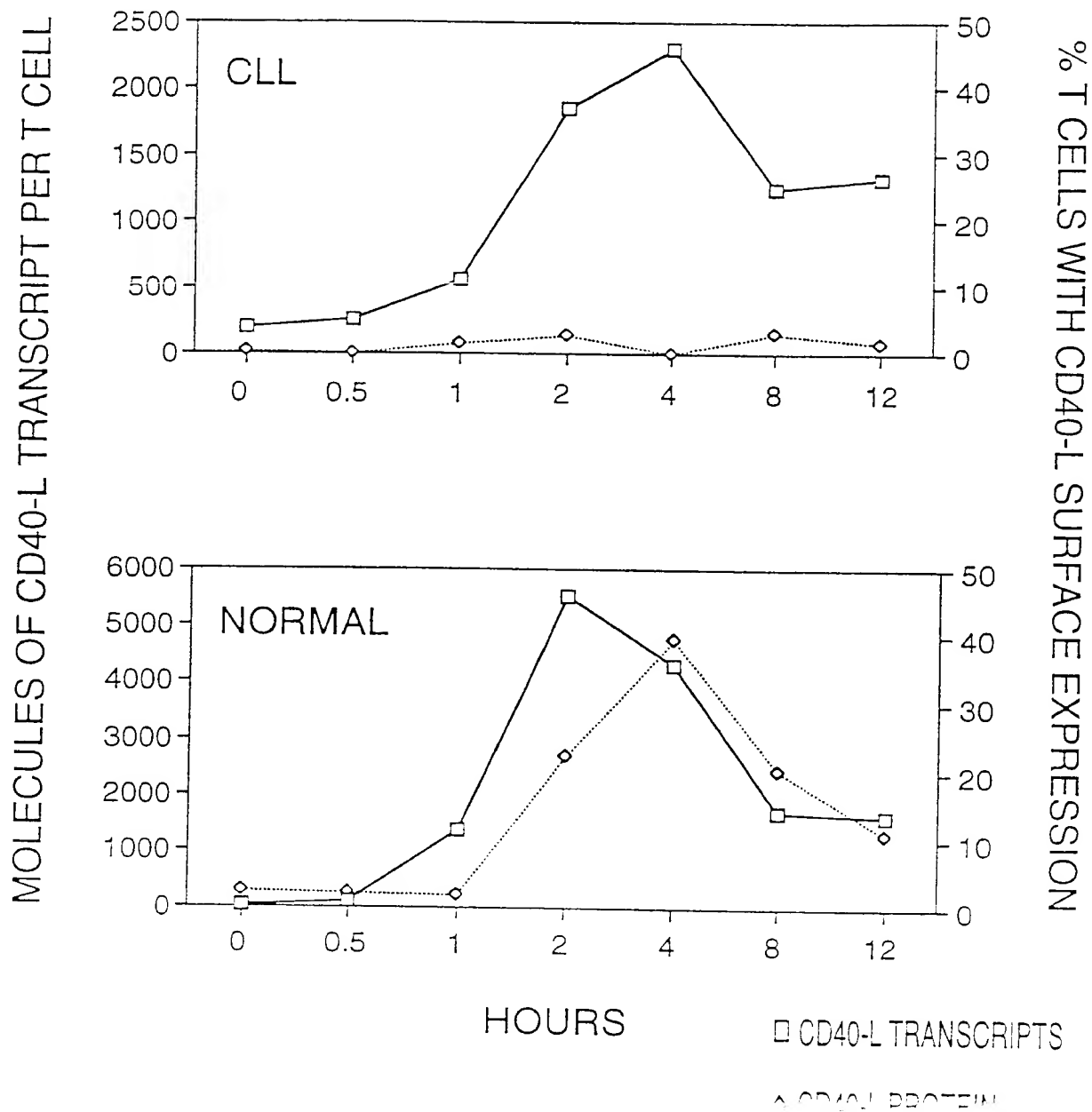
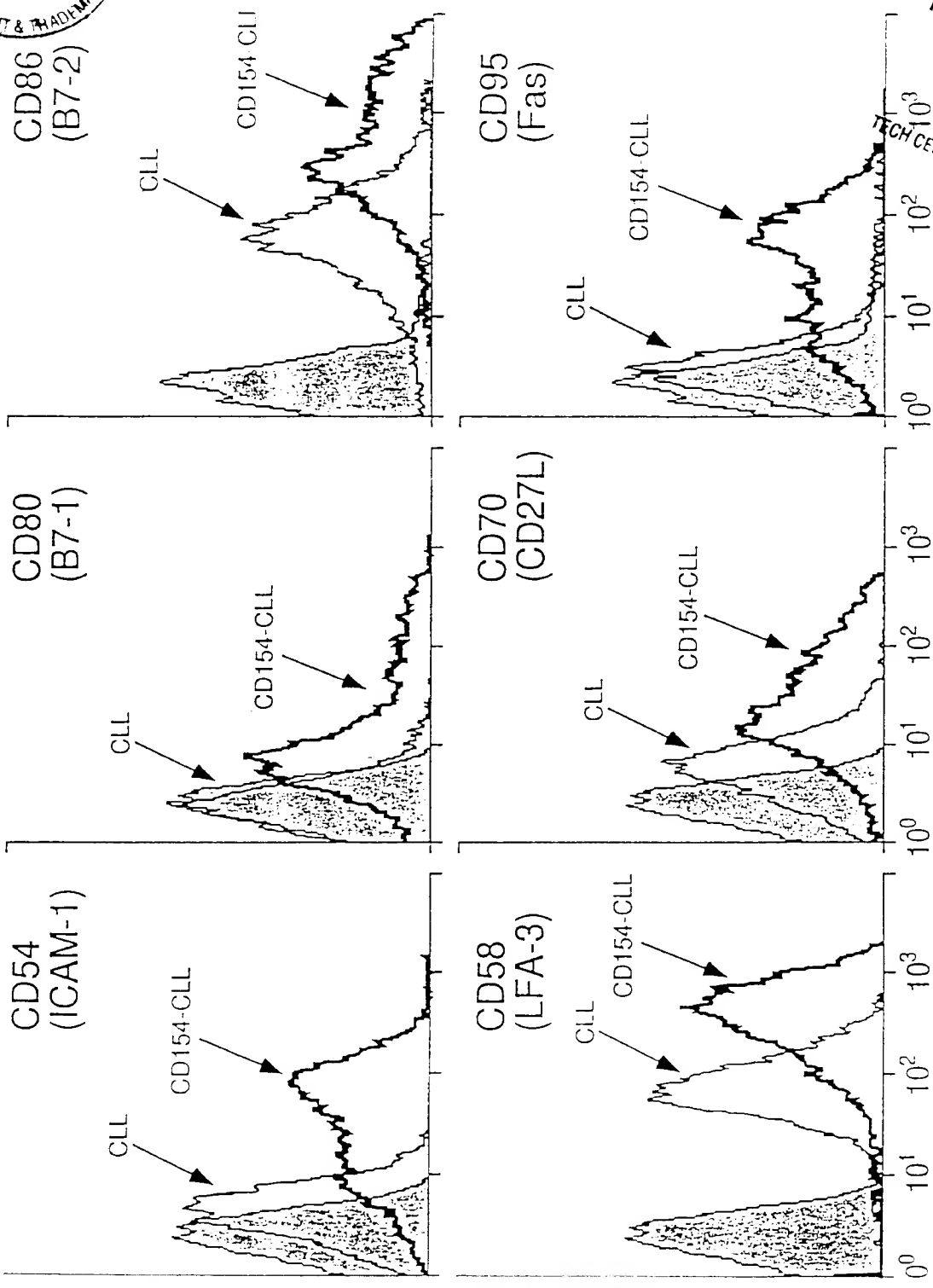


Figure 8



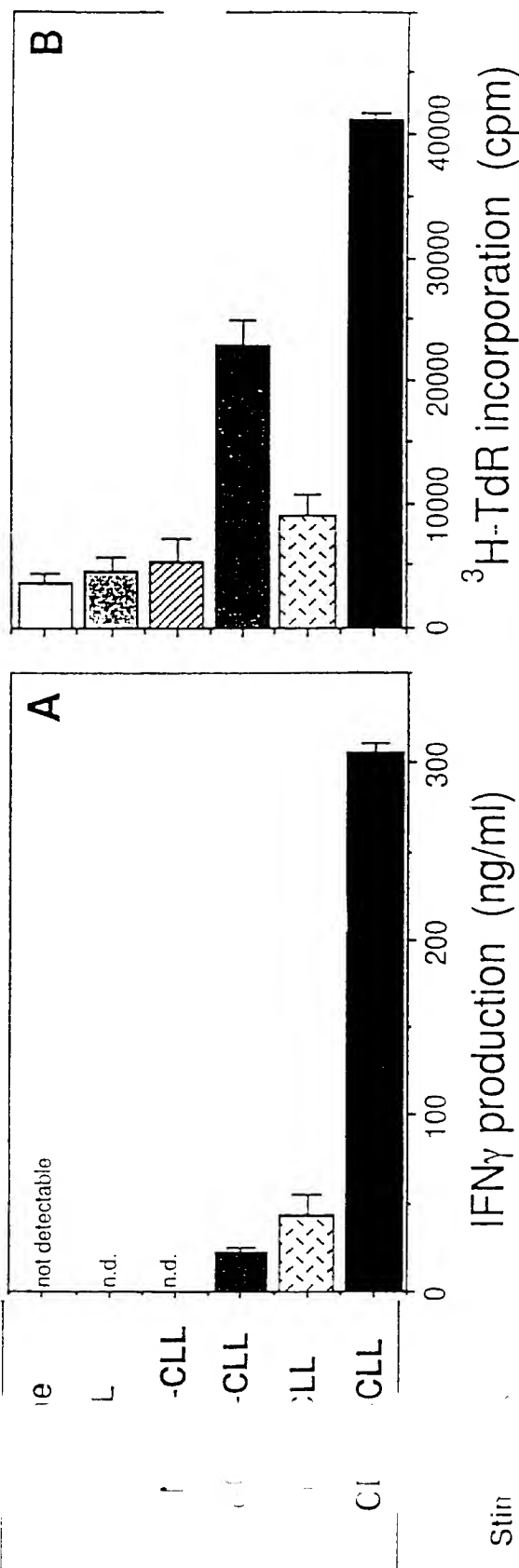
Green Fluorescence Intensity

june 10

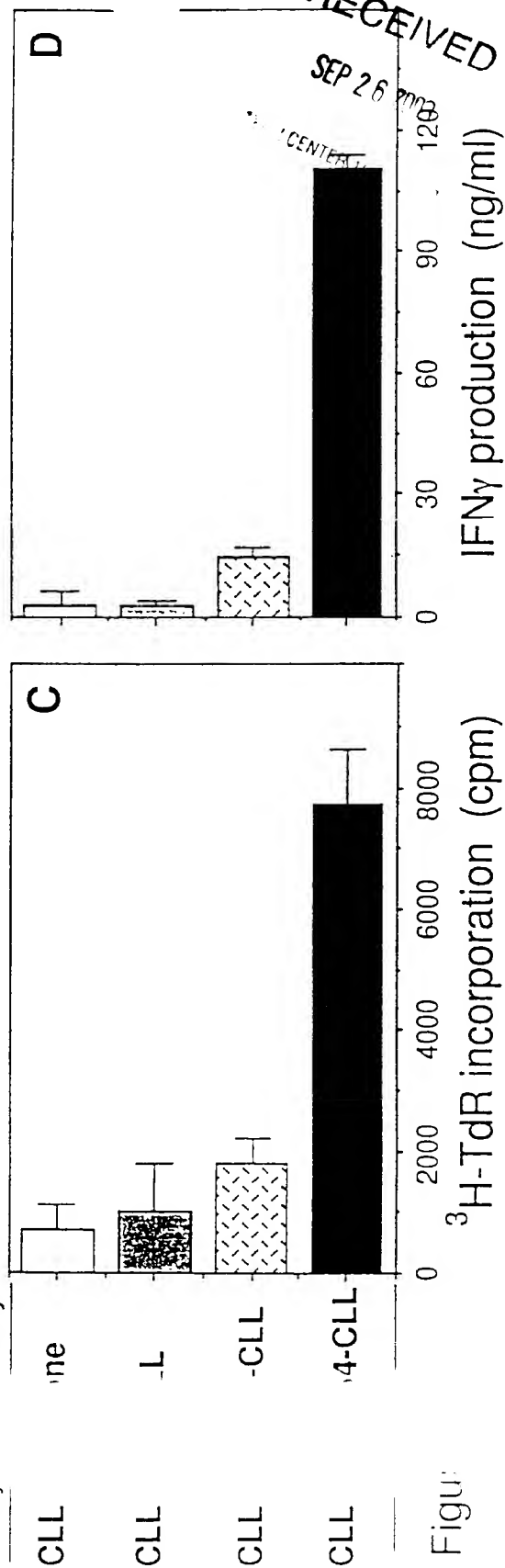
RECEIVED
 SEP 26 2003
 TECH CENTER 1600/2900



cell
 ed by



Stim
 Primary



Figure

RECEIVED
 SEP 26 2003
 CENTRAL

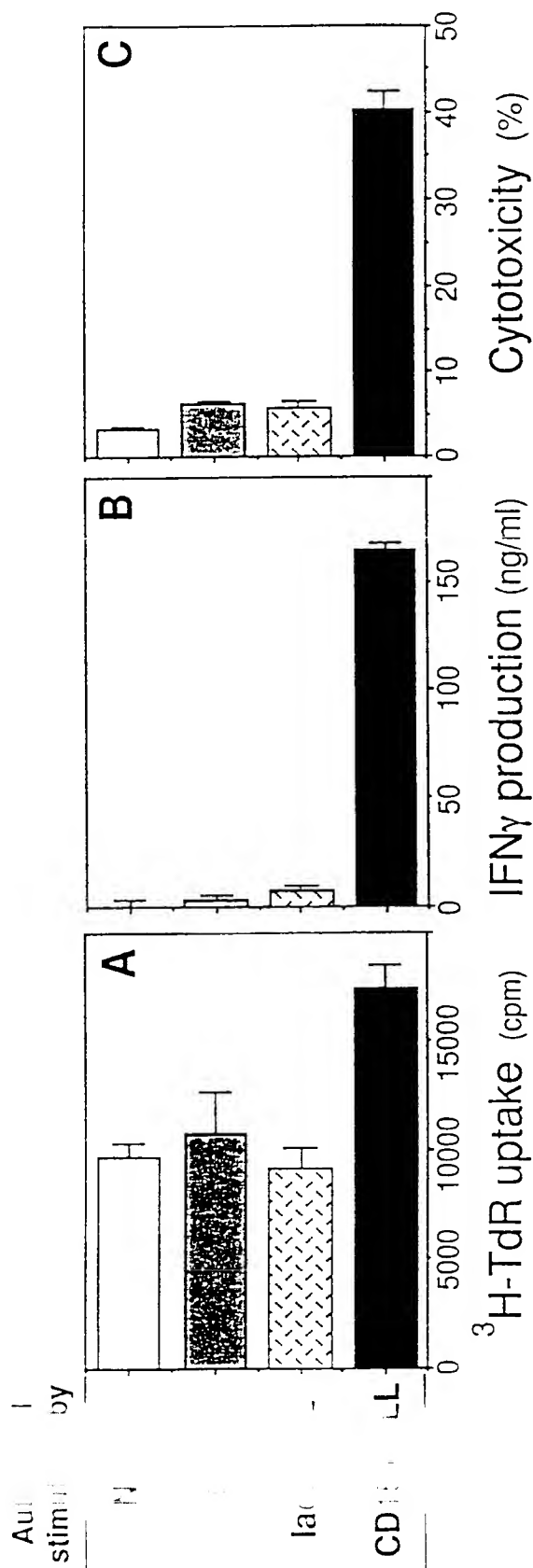
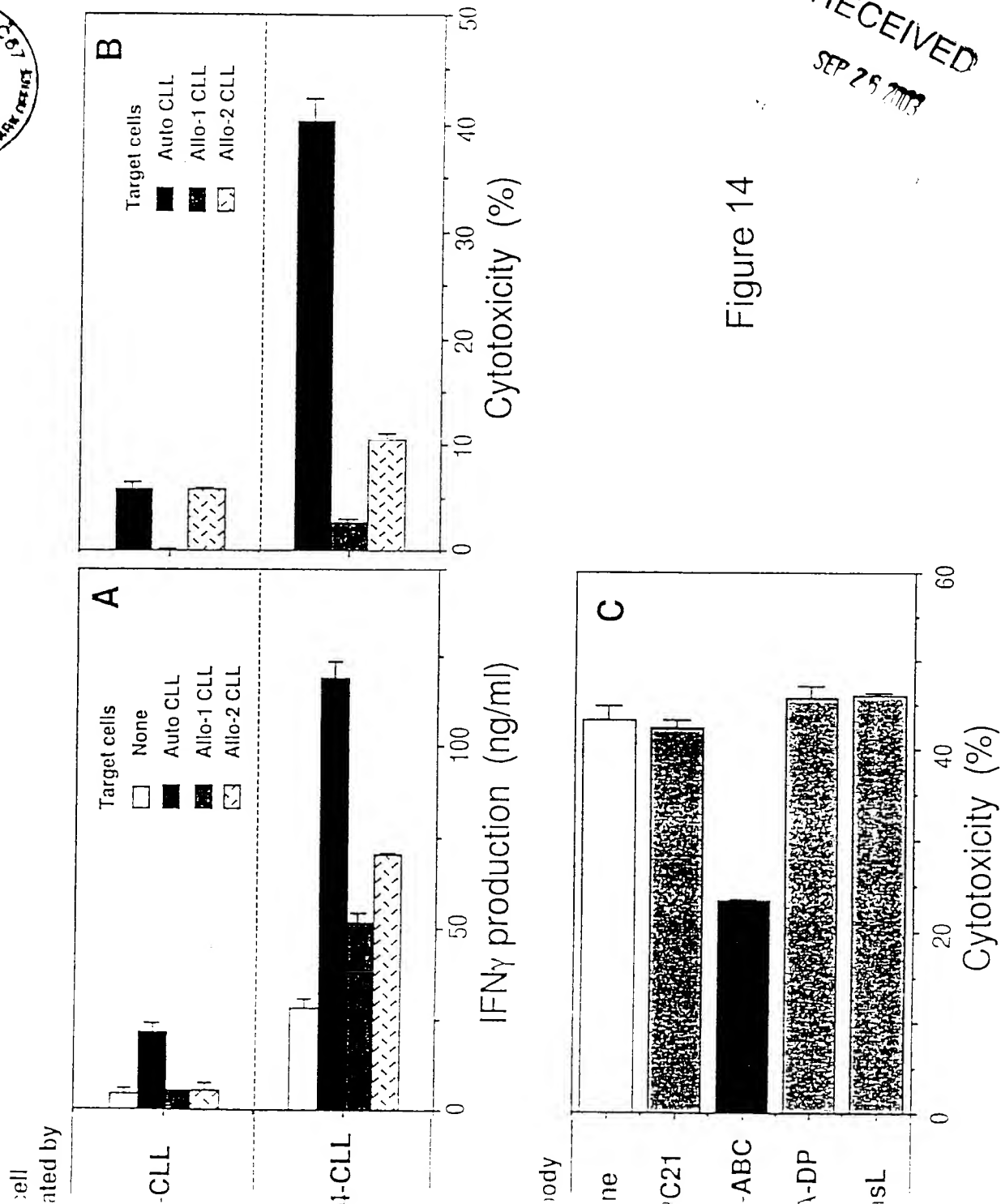


Figure 13

RECEIVED
 SEP 26 2003
 TECHNICAL STAFF 2906



RECEIVED
 SEP 25 2003

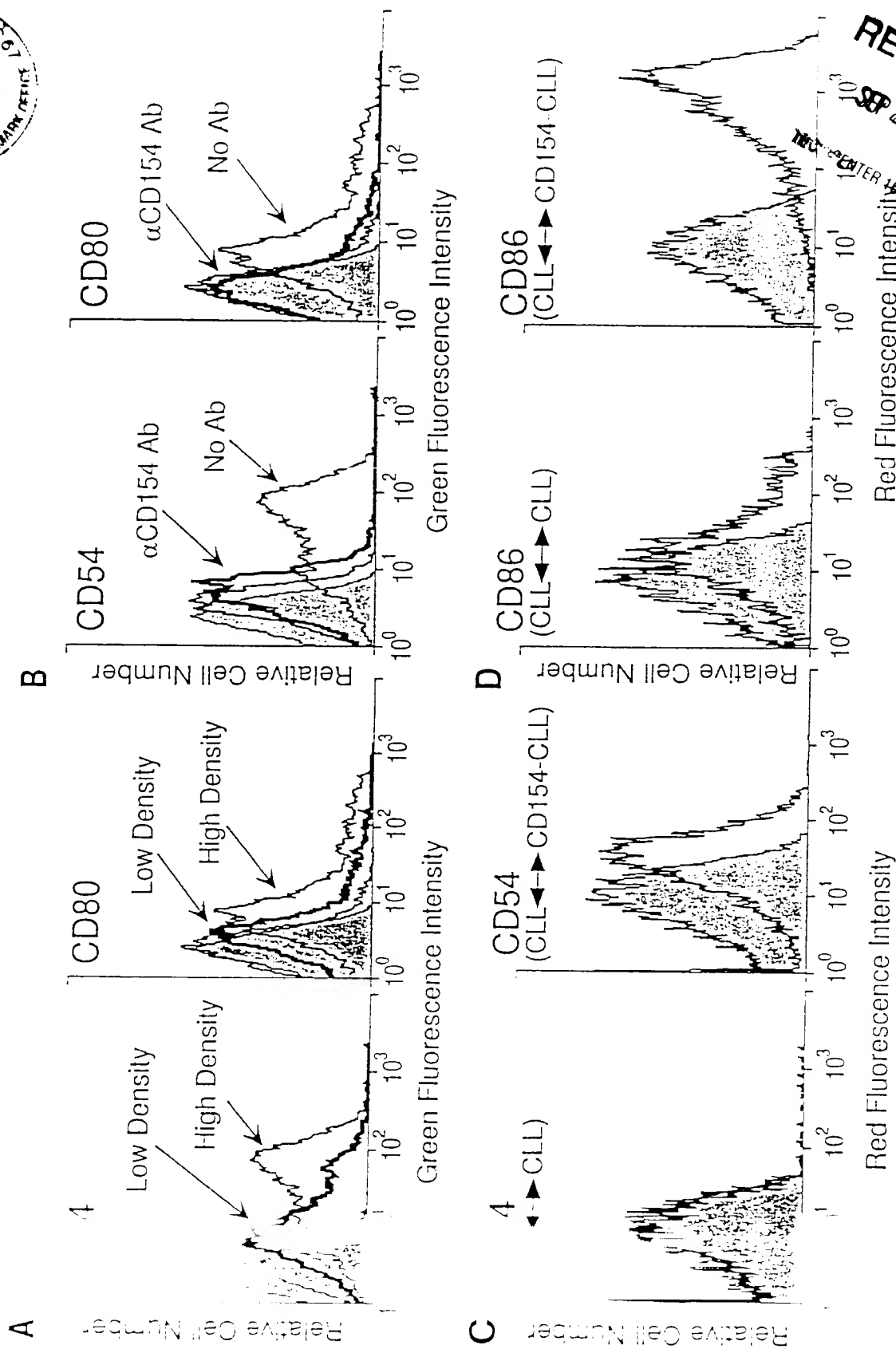


Figure 15

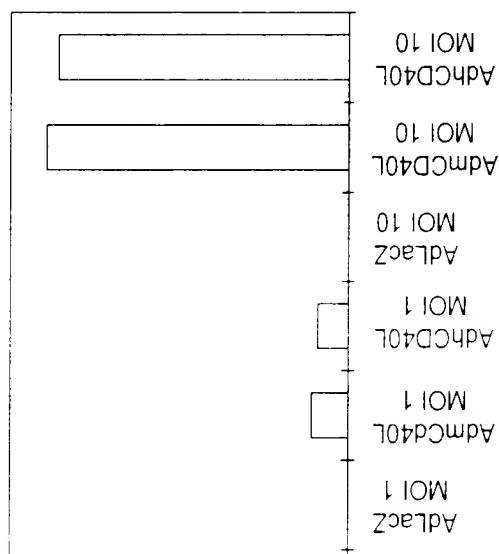
RECEIVED
 SEP 2 5 2003
 PATENT & TRADEMARK OFFICE



A

% CD40L Expression

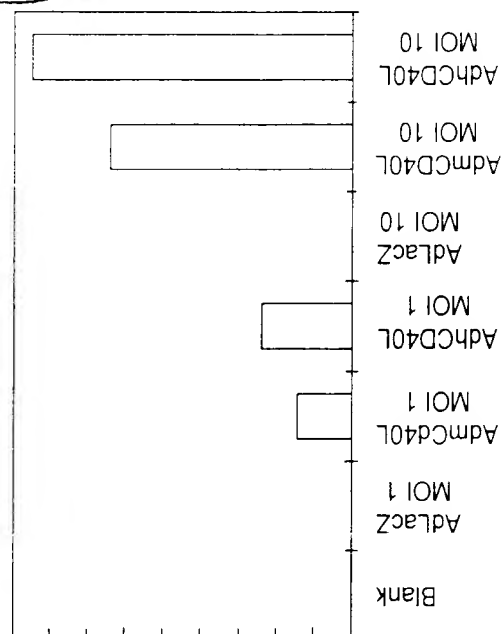
HeLa Cells



B

% CD40L Expression

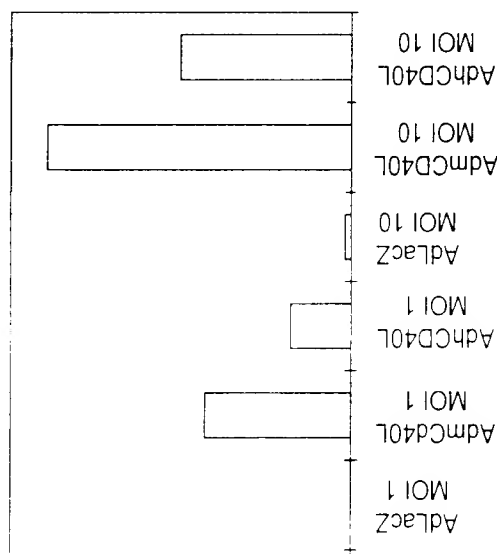
A427 Lung CA (CD40-)



C

% CD40L Expression

NCI 460 Large Cell CA (CD40+)



D

% CD40L Expression

SK-Mes-1 Squamous Cell (CD40++)

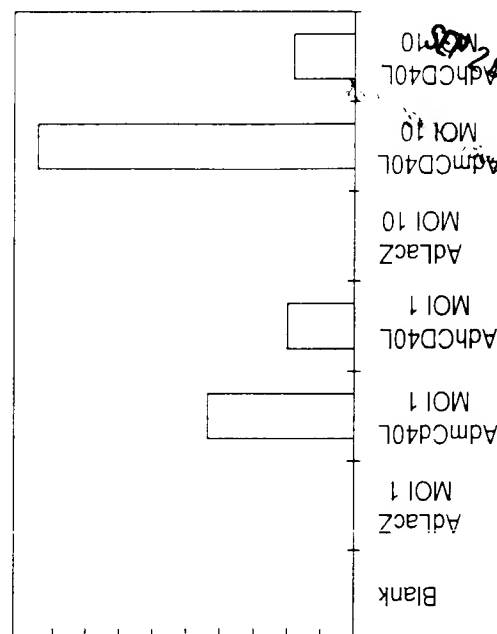
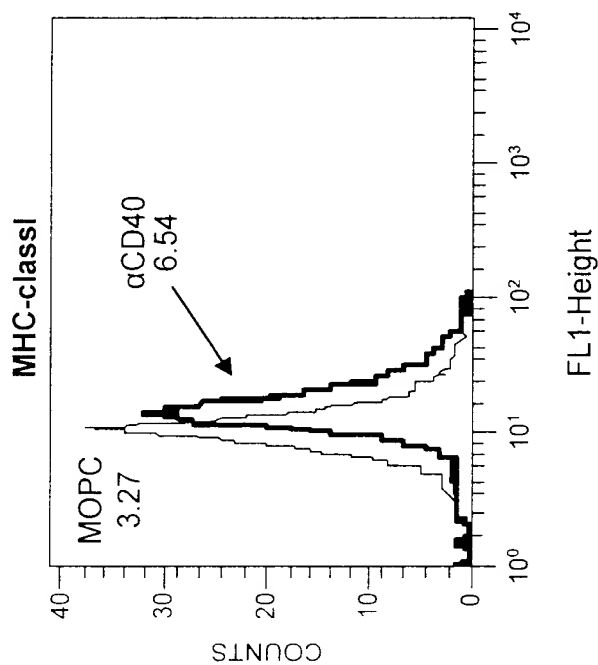
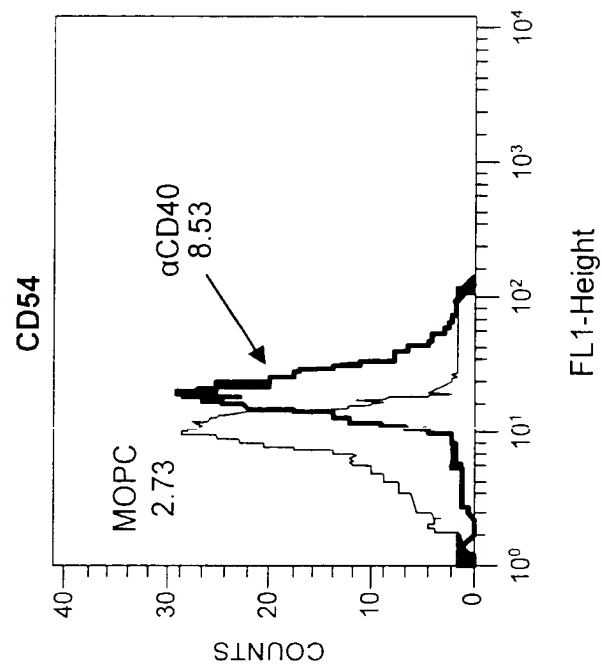
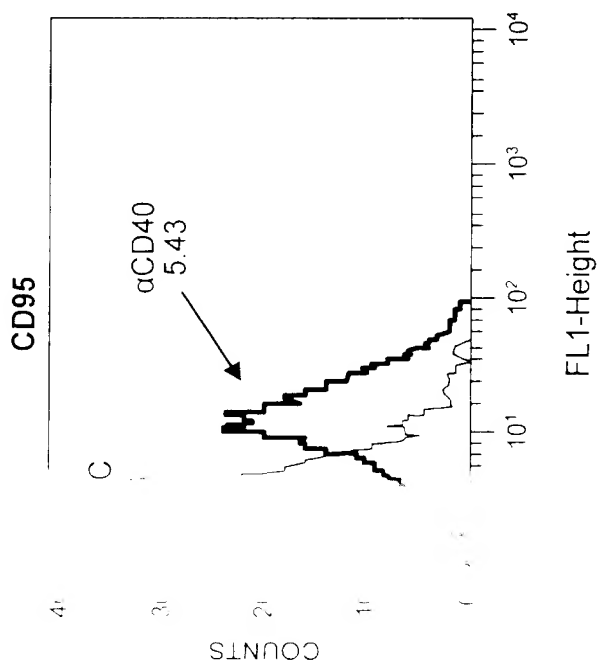


Figure 21

RECEIVED
 SEP 25 2003
 2002 9 25 2003



A

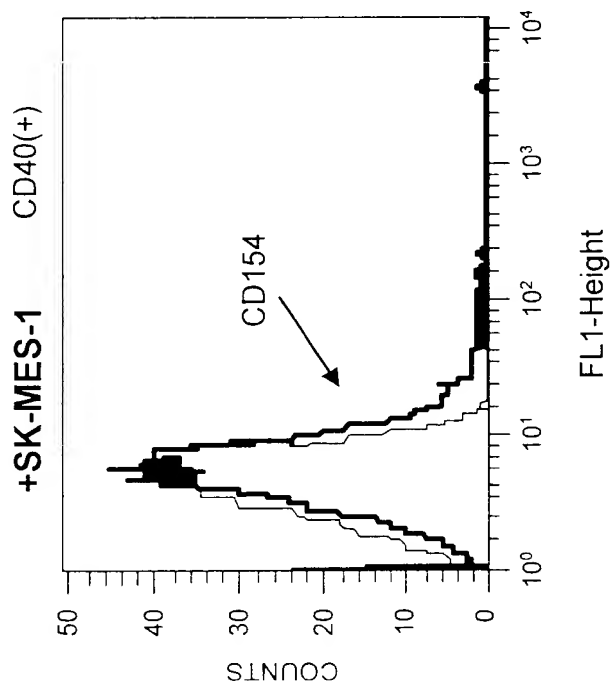
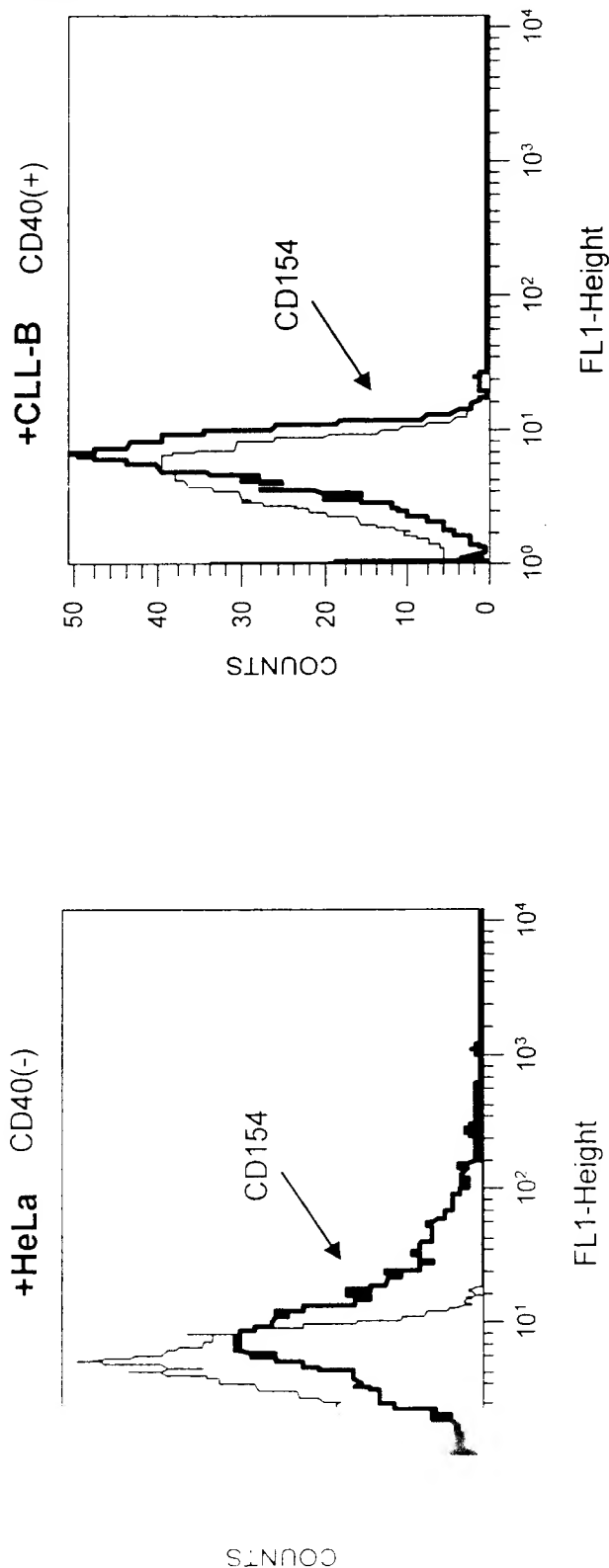


re 22a

RECEIVED
 SEP 26 2003
 TECH CENTER



B



ure 22b

RECEIVED
SEP 26 2003
TECH CENTER 1600/2906



RECEIVED
SEP 26 2003
TECH CENTER 1000/2500

RA SYNOVIAL FLUID AND PLASMA INHIBITION OF FAS-LIGAND

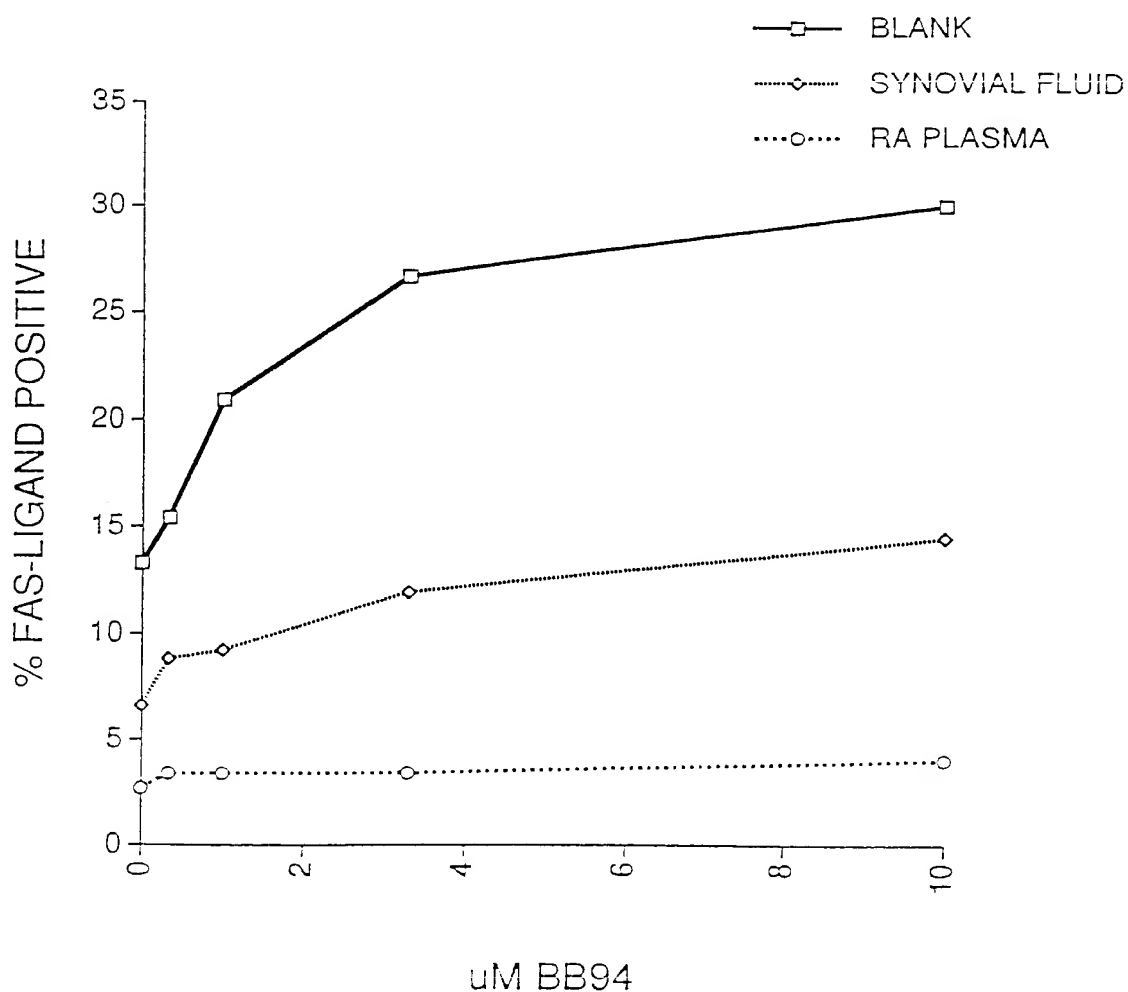


Figure 23



Gene Therapy of Leukemia

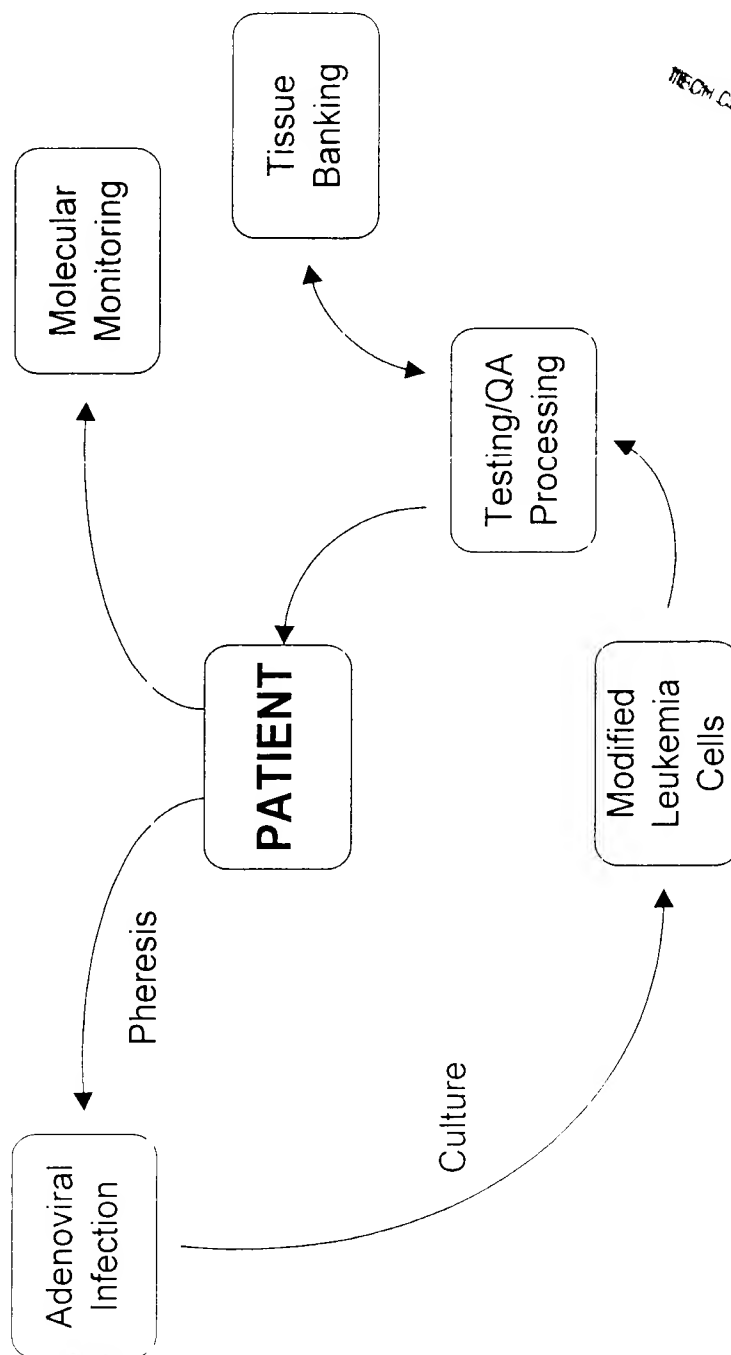


Figure 24

RECEIVED
SEP 26 2003
TECH CENTER 1600/2303

Cleavage

$$p_3 \quad p_2 \quad p_1 \quad p'_1 \quad p'_2 \quad p'_3 \quad p'_4$$

Interstitial Collagenase

P ₃	P ₂	P ₁	P' ₁	P' ₂	P' ₃	P' ₄
Pro	Leu	Gly	Met	Arg	Met/Ala	Arg
Leu	Met/Tyr	His	Leu	Leu	Gly	Lys
Ala	Val/Gly	Glu	Ile	Phe	Val	Gln
Asp	Ile	Tyr	Gln	Trp	Ser	Ile
Ser	Gln/Arg	Ala	Pro	Glu	Glu	Gly
Glu	Asp	Phe	Phe	Ala	Phe	Ser
Gly	Glu	Gln	Ala	Val/Gly	Arg	Glu
Arg	Ala	Asn	Tyr/Val	Ser	Pro	Ala

Neutrophil Collagenase

P ₃	P ₂	P ₁	P'	P' ₂	P' ₃	P' ₄
Pro	Leu	Glu	Tyr	Ala	Gly	Arg
Leu	Gln	Gly/His	Ile	Leu	Met	Gln
		Ala	Leu	Trp	Ala	
			Val			
			Phe			

Arg
same as MMP-1)

Figure 28A

RECEIVED

SEP 25 2003

1600/2900



RECEIVED
SEP 26 2003

TECH CENTER 1600/2200

NOVEL EXPRESSION VECTORS CONTAINING ACCESSORY MATERIALS
LIGANDS AND THEIR USE FOR IMMUNOMODULATION AND
TREATMENT OF MALIGNANCIES AND AUTOIMMUNE DISEASES
Inventor(s): Thomas Kropp, et al.; Serial No.: 08/982,272
Filing Date: December 1, 1997; Atty: Docket No.: 041673-2069

Gelatinases

MMMP-2 Gelatinase A

P ₄	P ₃	P ₂	P ₁	P' ₁	P' ₂	P' ₃	P' ₄
Gly	Pro	Arg	Gly	Leu	Ala/Leu	Gly/Ala	Gln
Ile	Ala	Gln	Asn	Ile/Phe	Phe/Trp	Leu	Arg
Pro	Arg	Leu	Ala	Val/Met	Gly	Ser	His
Arg	Ala	Ala	His	Ala	Arg/Gln	Pro	Pro
Leu	Lys	Ile	Leu	Glu	His		
	His	Tyr	Gln/Asn		Val		

MMMP-9 Gelatinase B

P ₄	P ₃	P ₂	P ₁	P' ₁	P' ₂	P' ₃	P' ₄
Gly	Pro	Arg	Gly	Leu	Glu	Ala	Thr
		Gln		Ile/Phe	Ala/Leu/Phe	Leu	
		Leu		Val/Met	Trp/Gly	Ser	
				Ala		Gly	

Stromelysins

MMMP-3 Stromelysin 1

P ₄	P ₃	P ₂	P ₁	P' ₁	P' ₂	P' ₃	P' ₄
Asp	Pro	Phe	Glu	Leu	Arg	Ala	Thr
Gly	Ala	Leu/Met	Ala	Phe	Leu/Phe	Arg/Met	
Ile/Arg				Trp/Tyr	Trp	Gly	Pro
Leu	Val	Tyr	Gln/Phe	Ile	Val	Val/Ile	
	Leu	Pro/Gly/Glu	Asn				
Ile/Val				Val	Gln	Ser/Asn	Ala
Leu	Thr	Ile	His	Met	His/Met	Glu/Thr	
Asp	Phe	Ala	Gly				
Ile/Asp	Arg	Ser	Leu/Pro	Glu	Glu/Ser/Thr	Leu	
Ile							
Ile/Lys/Phe							
Ile/Met	Ser/Gly						
Ile/Phe/Gln							

Figure 28B



0 Stromelysin 2

P₃
Ala
Pro

P₂
Ile
His

P₁
His
Leu

P'₁
Ile
Leu

P'₂
Gln
Val

P'₃
Ala
Glu

P'₄
Glu
Ala

5

Matrilysin

P₃
Pro
Leu

P₂
Leu
Gln
Val

P₁
Glu
Met/Ala
Pro/Gln
Gly

P'₁
Leu
Ile
Met

P'₂
Arg
Met
Gln

P'₃
Ala
Val/Arg/Met
Gly

P'₄
Gln

Figure 28C

RECEIVED
 SEP 26 2003
 TECH ST